Hemostasis Innovation is Here.

HEMOSIL®
D-DIMER HS 500

For the exclusion of

Deep venous thrombosis and pulmonary embolism



werfen

D-dimer
in clinical practice

In the diagnosis of DVT and PE

Diagnosis of venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), often begins with a clinical evaluation, followed by D-dimer testing. Confirmatory tests generally involve imaging techniques. For DVT, these are proximal lower extremity or whole-leg ultrasound. For PE, imaging tests are computed tomography pulmonary angiography (CTPA) or ventilation-perfusion (VQ) scan.

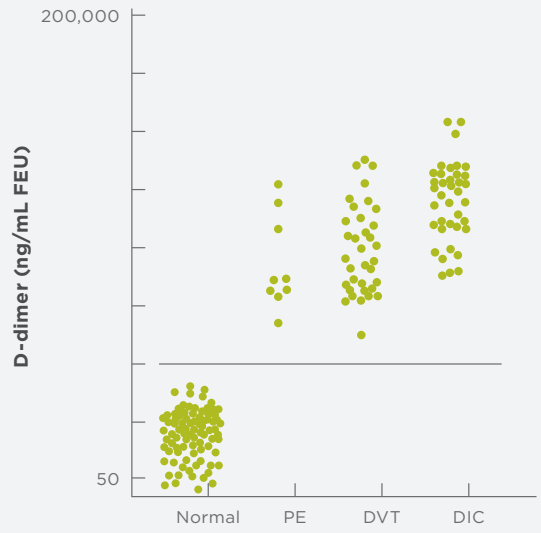
A substantial number of publications report the use of D-dimer, together with a pre-test probability (PTP) assessment model or score, as a safe, cost-effective management strategy for the evaluation of patients presenting with clinically-suspected VTE. This approach allows DVT and/or PE to be excluded in outpatients with suspected VTE who have a low or moderate PTP and a negative D-dimer, reducing the number of imaging tests required.[1–3]

Other clinical applications

D-dimer testing has been evaluated in a number of clinical applications, such as predictive factors, for recurrences of VTE after discontinuation of oral anticoagulant therapy and as an indicator of pregnancy complications.[4,5] D-dimer testing is also included in definitions of clinical laboratory criteria for the diagnosis and staging of disseminated intravascular coagulation (DIC).[6,7] Other studies suggest that elevated D-dimer levels in the normal population may indicate the risk for thrombosis.[8]

Further, D-dimer levels rise with age[2] and age-adjusted cut-off values for VTE exclusion have been shown to increase specificity and reduce the number of unnecessary imaging studies in patient populations greater than 50 years.[9–12]

D-dimer levels in VTE and DIC patient groups vs. normal subjects*



In patients with PE, DVT and DIC, D-dimer levels are greater than the establish cut-off value or reference range.

*Data on file, Werfen.

HemosIL D-Dimer HS 500

Liquid and ready to use, HemosIL D-Dimer HS 500 is a fully automated, latex-enhanced immunoassay for the exclusion of VTE in outpatients suspected of PE and DVT, in conjunction with a clinical PTP assessment model, on the ACL TOP and ACL TOP Family 50 Series Hemostasis Testing Systems.

The latex reagent is a suspension of polystyrene latex particles of uniform size, coated with the $F(ab')_2$ fragment of a monoclonal antibody, highly specific for the D-dimer domain included in fibrin degradation products or derivatives.

The use of the $F(ab')_2$ fragment allows for more specific D-dimer detection, minimizing interference from certain endogenous factors, such as rheumatoid factor.

The assay is optimized for a wavelength of 671 nm, providing a very high analytical sensitivity, enhanced working range and minimized interference from hemoglobin.

Saves time and resources	Enhances patient care
Optimizes laboratory workload • Liquid, ready-to-use • Fully automated **Provides rapid patient response** • Results in <5 minutes **Reduces number of unnecessary imaging techniques** • High specificity and sensitivity for VTE	**Cleared by regulatory authorities for the exclusion of VTE with superior accuracy and precision** • 100% negative predictive value (NPV) • In conjunction with a PTP score, excludes DVT and PE using a cut-off value of 500 ng/mL FEU • Minimized interference from rheumatoid factor and hemoglobin

HemosIL D-Dimer HS 500, with a PTP Score, safely excludes DVT and PE

Using a cut-off of 500 ng/mL FEU, HemosIL D-Dimer HS 500 successfully excluded DVT and PE in over 1,000 patients (two clinical studies), with an NPV of 100% and sensitivity of 100%.

Single-center management study	Multicenter management study
• 295 outpatients • NPV = 100% • Specificity for VTE = 42.3%	• 747 outpatients • NPV = 100% • Specificity for DVT = 42.1% • Specificity for PE = 48.3%

VTE management studies with HemosIL D-Dimer HS 500

Simple, proven and efficient

Enhancing diagnosis of DVT and PE

An outcome study was performed on 295 samples from patients suspected of PE or DVT (25.4% frequency of VTE). Positive results were confirmed through standard imaging techniques.

Results, below, are based on a cut-off value of 500 ng/mL FEU for HemosIL D-Dimer HS 500, the ELISA method, and 230 ng/mL DDU for HemosIL D-Dimer HS.

VTE Performance	HemosIL D-Dimer HS 500	HemosIL D-Dimer HS	ELISA
Samples (n)	295	295	295
Sensitivity (%) (95% CI)	**100** (95.2–100)	**100** (95.2–100)	**100** (95.2–100)
Specificity (%) (95% CI)	**42.3** (35.7–49.1)	**45.5** (38.7–52.3)	**35** (28.7–41.7)
NPV (%) (95% CI)	**100** (96.1–100)	**100** (96.4–100)	**100** (95.3–100)

Multicenter management study

Excluding DVT and PE

A multicenter management study was performed at four hospitals on 747 samples from patients suspected of DVT (n=401) or PE (n=346). Patient management was based on a study-specific diagnostic algorithm involving PTP scoring.

DVT and PE patients were confirmed through standard imaging techniques. Patients with negative results completed a three-month follow-up. Results, below, are based on a cut-off value of 500 ng/mL FEU.

DVT Performance	All samples	High PTP	Low + moderate PTP
Samples (n)	401	79	322
Sensitivity (%) (95% CI)	**100** (96–100)	**100** (92.1–100)	**100** (92.1–100)
Specificity (%) (95% CI)	**42.1** (36.6–47.8)	**32.4** (17.4–50.5)	**43.3** (37.4–49.4)
NPV (%) (95% CI)	**100** (97.2–100)	**100** (71.5–100)	**100** (97–100)

PE Performance	All samples	High PTP	Low + moderate PTP
Samples (n)	346	24	322
Sensitivity (%) (95% CI)	**100** (93.2–100)	**100** (66.4–100)	**100** (91.8–100)
Specificity (%) (95% CI)	**48.3** (42.5–54.2)	**33.3** (11.8–61.6)	**49.1** (43.1–55.1)
NPV (%) (95% CI)	**100** (97.4–100)	**100** (47.8–100)	**100** (97.3–100)

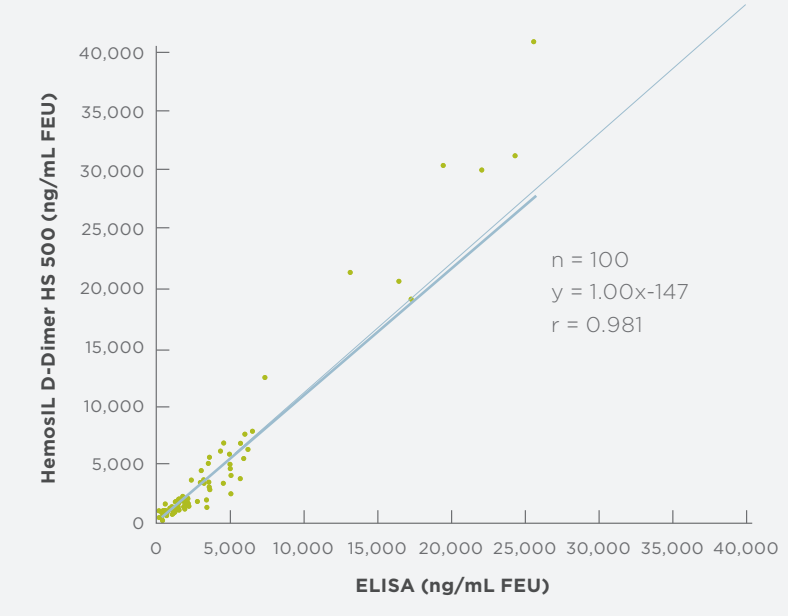
Analytical performance on the ACL TOP Family and ACL TOP Family 50 Series

Linearity	Up to 7,650 ng/mL FEU without rerun Up to 128,000 ng/mL FEU with automated rerun		
Precision	**ACL TOP Family**	**Mean (ng/mL FEU)**	**% CV (Total)**
	Plasma Pool	423	9.5
	Low D-Dimer Control	877	8.9
	High D-Dimer Control	2,469	7.3
	Level 1 D-Dimer Control	559	4.8
	Level 2 D-Dimer Control	1,908	2.2
	ACL TOP Family 50 Series		
	Plasma Pool	301	9.6
	Low D-Dimer HS 500 Control	675	4.3
	High D-Dimer HS 500 Control	2,779	2.1
Detection Limit	203 ng/mL FEU		
Interferences		**None up to:**	
	Hemoglobin	500 mg/dL	
	Bilirubin	18 mg/dL	
	Triglycerides	1,327 mg/dL	
	Rheumatoid factor	1,400 IU/mL	
	Human anti-mouse antibody (HAMA)	Formulation contains blocking agent	
Stability of Opened Reagents	Latex Reagent	1 month at 2–8˚C	
	Buffer	1 month at 2–8˚C	
	Calibrator	1 month at 2–8˚C	
Onboard Stability	Latex Reagent	7 days at 15˚C	
	Buffer	7 days at 15˚C	
	Calibrator	3 days at 15–25˚C	

Method comparison

Excellent correlation

A comparison study of HemosIL D-Dimer HS 500 vs. ELISA, on samples from outpatients suspected of VTE, demonstrated excellent correlation and slope.



HemosIL D-Dimer HS 500 Kit Composition

Product	Part Number	Kit Configuration
D-Dimer HS 500	0020500100	3 x 4 mL Latex Reagent (liq) 3 x 6 mL Reaction Buffer (liq) 2 x 1 mL Calibrator (lyo)
D-Dimer HS 500 Controls*	0020013100	5 x 1 mL Level 1 D-Dimer HS 500 control (liq) 5 x 1 mL Level 2 D-Dimer HS 500 control (liq)
D-Dimer HS 500*	0020500300	4 x 13.5 mL Latex Reagent (liq) 4 x 16 mL Reaction Buffer (liq) 1 x 1 mL Calibrator (lyo)
D-Dimer HS 500 Controls*	0022550030	5 x 1 mL Level 1 D-Dimer HS 500 control 5 x 1 mL Level 2 D-Dimer HS 500 control

*Not available in all countries.

References

1. Legnani C, Cini M, Scarvelis D, Toulon P, Wu JR, Palareti G. Multicenter evaluation of a new quantitative highly sensitive D-dimer assay, the HemosIL D-dimer HS 500, in patients with clinically suspected venous thromboembolism. *Thrombosis Research.* 2010;125(5):398–401.
2. CLSI. Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline. CLSI Document H59-A. Wayne, PA: Clinical and Laboratory Standards Institute. 2011.
3. Verma K, Legnani C, Palareti G. Cost-minimization analysis of venous thromboembolism diagnosis: comparison of standalone imaging with a strategy incorporating D-dimer for exclusion of venous thromboembolism. *Res Pract Thromb Haemost.* 2017;00:1–5.
4. Nolan TE, Smith RP, Devoe LD. Maternal plasma D-dimer levels in normal and complicated pregnancies. *Obstetrics & Gynecology.* 1993;81(2):235–238.
5. Legnani C, Palareti G, Cosmi B, Cini M, Tosetto A, Tripodi A, et al. Different cut-off values of quantitative D-dimer methods to predict the risk of venous thromboembolism recurrence: a post-hoc analysis of the PROLONG study. *Haematologica.* 2008;Jun;93(6):900–907.
6. Toh CH, Hoots WK, SSC on Disseminated Intravascular Coagulation of the ISTH. The scoring system of the Scientific and Standardisation Committee on Disseminated Intravascular Coagulation of the International Society of Thrombosis and Haemostasis: a 5-year overview. *J Thromb Haemost.* 2007;5:604–606.
7. Wada H, Thachil J, Di Nisio M, Mathew P, Kurosawa S, Gando S, et al. Guidance for diagnosis and treatment of disseminated intravascular coagulation from harmonization of the recommendations from three guidelines. *J Thromb Haemost.* 2013;11:761–767.
8. Cushman M, Folsom AR, Wang L, Aleksic N, Rosamond WD, Tracy RP, et al. Fibrin fragment D-dimer and the risk of future venous thrombosis. *Blood.* 2003;101(4):1243–1248.
9. Righini M, Righini M, Van Es J, Den Exter PL, Roy P, Verschuren F, Ghuysen A, et al. Age-Adjusted D-Dimer Cutoff Levels to Rule Out Pulmonary Embolism. *JAMA.* 2014;311 1117–1124.
10. Cini M, Legnani C, Frascaro M, Sartori M, Cosmi B, Palareti G. D-dimer use for deep venous thrombosis exclusion in elderly patients: a comparative analysis of three different approaches to establish cut-off values for an assay with results expressed in D-dimer units. *Int J Lab Hematol.* 2014;36:541–547.
11. Schouten H, Geersing GJ, Koek HL, Zuithoff NPA, Janssen KJM, Douma RA, et al. Diagnostic accuracy of conventional or age adjusted D-Dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. *BMJ.* 2013;346:2492.
12. Mullier F, Vanpee D, Jamart J, Dubuc E, Bailly N, Douxfils J, et al. Comparison of five D-dimer reagents and application of an age-adjusted cut-off for the diagnosis of venous thromboembolism in emergency department. *Blood Coagul Fibrinolysis.* 2014;25:309–315.
13. De Pooter N, Brionne-François M, Smahi M, Abecassis L, Toulon P. Age-adjusted D-dimer cut-off levels to rule out venous thromboembolism in patients with non-high pre-test probability: Clinical performance and cost-effectiveness analysis. *J Thromb Haemost.* 2021;19(5):1271-1282. doi: 10.1111/jth.15278

Additional Literature

- Arza B, Sanchez T, del Toro L, Sales M, Arnout J. Performance of a new turbidimetric D-Dimer assay adapted to automated coagulometers. *Journal of Thrombosis and Haemostasis.* 2009; Volume 7, supplement 2: Abstract PP-WE-525.
- Bounameaux H, de Moerloose P, Perrier A, Reber G. Plasma measurement of D-Dimer as diagnostic aid in suspected venous thromboembolism: an overview. *Thrombosis and Haemostasis.* 1994;71(1):1–6.
- Gaffney PJ, Creighton LJ, Callus M, Thorpe R. Monoclonal antibodies to crosslinked fibrin degradation products (XL-FDP) II, Evaluation in a variety of clinical conditions. *British Journal of Haematology.* 1988;68:91–96.
- Kappert G, Halimeh S, Rott H. Reference ranges for the determination of D-dimers in pregnancy. *Journal of Thrombosis and Haemostasis.* 2009; Volume 7, Supplement 2: Abstract PP-WE-370.
- Nieuwenhuizen W. A Reference Material for Harmonisation of D-Dimer Assays. *Thrombosis and Haemostasis.* 1997;77(5):1031–1033.
- Perrier A, Nendaz MR, Sarasin FP, Howarth N, Bounameaux H. Cost-Effectiveness Analysis of Diagnostic Strategies for Suspected Pulmonary Embolism Including Helical Computed Tomography. *Am J Respir Crit Care Med.* 2003;167:39–44.
- Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, Kovacs G, Mitchell M, Lewandowski B, Kovacs MJ. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N. Engl. J. Med.* 2003;349:1227–1235.

werfen.com

For more information, contact your local Werfen sales representative or distributor.

ACL, ACL AcuStar, ACL Elite, ACL TOP, HemoCell, HemoHub, HemosIL, ReadiPlasTin, RecombiPlasTin, SynthAFax, and SynthASil are trademarks of Instrumentation Laboratory (d.b.a. Werfen) Company and/or one of its subsidiaries or parent companies and may be registered in the United States Patent and Trademark Office and in other jurisdictions. The Werfen logo is a trademark of Werfen and may be registered in the Patent and Trademark Offices of jurisdictions throughout the world. All other product names, company names, marks, logos, and symbols are trademarks of their respective owners.

©2022 Instrumentation Laboratory. All rights reserved.

DDHS500 Bro EU IVDD/ROW Rev00 10.22